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| APPLICATION NO. | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
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| 10/774,192 | 02/06/2004 | John E. Sims | 2872-D | 7210 |

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| EXAMINER | |
|---|---|
| LOCKARD, JON MCCLELLAND | |
| **ART UNIT** | **PAPER NUMBER** |
| 1647 | |

DATE MAILED: 10/17/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

| Office Action Summary | Application No. | Applicant(s) | |
|---|---|---|---|
| | 10/774,192 | SIMS ET AL. | |
| | Examiner | Art Unit | |
| | Jon M. Lockard | 1647 | |

*-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --*

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

1)☒ Responsive to communication(s) filed on *02 August 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

4)☒ Claim(s) *18-26* is/are pending in the application.

4a) Of the above claim(s) *20* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18,19 and 21-26* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *18-26* are subject to restriction and/or election requirement.

**Application Papers**

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *6/20/05*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

## DETAILED ACTION

### *Election/Restrictions*

1. Applicant's election without traverse of Group I, claims 18 and 19, and newly added claims 21-26, drawn to a method for blocking $NF_KB$/JNK activation in a mammal comprising administering to said mammal an antibody that binds to a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7, in the reply filed on 02 August 2006 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

2. Claim 20 is withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on 02 August 2006. The restriction requirement is still deemed proper and is therefore made **FINAL**. Therefore, claims 18-26 are pending, and claims 18, 19, and 21-26 are under consideration and the subject of this Office Action.

### *Information Disclosure Statement*

3. The information disclosure statement (IDS) submitted on 20 June 2005 has been considered by the Examiner.

### *Biological Deposits*

4. The biological deposit of the 4E11 hybridoma cell line under accession No. HB 9259 is noted (See pg 15, lines 18-19) but is not required for enabling the claimed invention.

*Specification*

5. The disclosure is objected to because of the following informalities:

6. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested: "ACPL ANTIBODIES AND METHODS OF USE THEREOF".

7. The disclosure is objected to because it contains embedded hyperlinks and/or other form of browser-executable code. See for example, page 3, lines 14-17, pg 32, lines 23-24, 28, and 32-33, pg 53, lines 29-31 and pg 54, line 6. Applicant is required to delete the embedded hyperlinks and/or other form of browser-executable code. See MPEP § 608.01.

8. An updated status of the parent nonprovisional application should be included in the first sentence of the specification. A statement reading "This application is a continuation of U.S. application serial number 10/212,356, filed August 2, 2002, now U.S. Patent No. 6,692,740, which is a divisional of ..." should be entered.

*Sequence Rules*

9. This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, the application fails to comply with the requirements of 37 CFR 1.821 through 1.825. Specifically, amino acid sequences appear at lines 12-13 on page 15 of the specification (filed 06 February 2004) without an accompanying sequence identifier (i.e., SEQ ID NO: #). Applicant is required to provide (1) a substitute computer

readable form (CRF) copy of a "Sequence Listing" which includes all of the sequences that are present in the instant application and encompassed by these rules, (2) a substitute paper copy of that "Sequence Listing", (3) an amendment directing the entry of that paper into the specification, and (4) a statement that the content of the paper and computer readable copies are the same, and, where applicable, include no new matter, as required by 37 C.F.R. § 1.821 through 1.825. The instant specification will also need to be amended so that it complies with 37 C.F.R. § 1.821(d) which requires a reference to a particular sequence identifier (i.e., SEQ ID NO: #) be made in the specification and claims wherever a reference is made to that sequence (See M.P.E.P. 2422.04).

### *35 U.S.C. § 112, Second Paragraph*

10. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

11. Claims 18-19 and 21-26 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

12. Claim 18 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claim does not have a step that clearly relates back to the preamble. For example, the last line of the claim recites "wherein the antibody blocks IL-18 stimulation of $NF_KB$ signaling, whereas the preamble recites "a method for blocking $NF_KB$ activation".

13. Claim 19 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite because the claim does not have a step that clearly relates back to the preamble. For example, the last line of the claim recites "wherein the antibody blocks IL-18 stimulation of JNK signaling, whereas the preamble recites "a method for blocking JNK activation".

14. Claims 21-26 are rejected for depending from an indefinite claim.

***Claim Rejections - 35 USC § 112, 1st Paragraph (Scope of Enablement)***

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

15. Claims 18-19 and 21-26 are rejected under 35 U.S.C. § 112, first paragraph, because the specification, while being enabling for (1) a method for inhibiting or blocking IL-18 stimulation of $NF_KB$ activation in a mammal comprising administering to a mammal an antibody that binds a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7; and (2) a method for inhibiting or blocking IL-18 stimulation of JNK activation in a mammal comprising administering to a mammal an antibody that binds a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7, does not reasonably provide enablement for a method for blocking $NF_KB$/JNK activation that *is not* in response to IL-18 stimulation. Specifically, the specification does not reasonably provide enablement for (1) a method for blocking $NF_KB$ activation in a mammal comprising administering to a mammal an antibody that binds a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7; and (2) a method for blocking JNK activation in a mammal comprising

administering to a mammal an antibody that binds a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

16. The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

17. The claims are drawn very broadly to a method for blocking $NF_KB$/JNK activation comprising administering to a mammal an antibody that binds to a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7. Although the claims sets forth that the antibody blocks IL-18 stimulation of $NF_KB$/JNK signaling, the claims do not require that the $NF_KB$/JNK activation is the result of IL-18 stimulation and are drawn very broadly to blocking any means of $NF_KB$/JNK activation in a mammal. The specification teaches that the ACPL polypeptide of SEQ ID NO:7 is an IL-18 binding cofactor that is required for IL-18 mediated activation of $NF_KB$ and JNK activation (See pg 7, lines 22-23; pg 40, lines 1-9; Examples 6 and 7), and that the antibodies of the claimed methods can block $NF_KB$/JNK activation that is a result of IL-18 signaling (See pg 40, lines 29-31;

pg 56, lines 9-33). Thus, while the specification provides adequate guidance for the skilled artisan to make and use antibodies that bind a polypeptide consisting of amino acids 15-356 of SEQ ID NO:7 in a method of inhibiting and/or blocking IL-18 stimulation of $NF_KB$/JNK activation, it does not provide adequate guidance, nor is it at all predictable what effects that administration of the antibody of the claimed methods would have on $NF_KB$/JNK that are activated via pathways other than those mediated by IL-18, and it would require undue experimentation to determine such.

18. The art teaches that in addition to the activation of $NF_KB$ via the IL-18 pathway, the activity of $NF_KB$ is elicited by other pathways, including TNFα via the TNF receptor and IL-1 via the IL-1 receptor (See Bacher et al. Current Pharmaceutical Design. 10:2827-2837, 2004; see pg 2827-2828). Likewise, the art also teaches that in addition to the activation of JNK via the IL-18 pathway, JNK is also activated by other signaling pathways, including IL-22 via the IL-22R1/CRF2-4/IL10Rb receptor (See Lejeune et al. The Journal of Biological Chemistry. 37:33676-33682, 2002), TNF via the TNF receptor (See Wullaert et al., Biochemical Pharmacology. 72:1090-1101, 2006), and IL-1 via the IL-1 receptor (See Li et al., Proc. Natl. Acad. Sci. USA 98(8):4461-4465, 2001). Thus, while the specification teaches that the antibodies of the claimed methods can block $NF_KB$/JNK activation that is a result of IL-18 signaling, one skilled in the art would not expect, nor would they be able to predict that the administration of the antibodies in the claimed methods would block/inhibit all the potential pathways that lead to $NF_KB$/JNK activation.

19. Due to the lack of direction/guidance presented in the specification regarding whether or not the antibody of the claimed methods would block/inhibit any means of $NF_KB$/JNK activation; the breadth of the claims; and the unpredictability of the art which establishes that there are multiple pathways involved in the activation of $NF_KB$/JNK; it would require undue experimentation and making a substantial inventive contribution for the skilled artisan to discover how to make and/or use the Applicants' invention in its full scope.

***Summary***

20. No claim is allowed.

21. The art made of record and not relied upon is considered pertinent to applicant's disclosure.

Debets et al. (2000). IL-18 receptors, their role in ligand binding and function: anti-IL-1RAcPL antibody, a potent antagonist of IL-18. The Journal of Immunology. 165:4950-4956.

Gillespie et al. (1998). Interleukin-18: perspectives on the newest interleukin. Cytokine and Growth Factor Reviews. 9(2):109-116.

Adachi et al. (1998). Targeted disruption of the *MyD88* gene results in loss of IL-1- and IL-18-mediated function. Immunity. 9:143-150.

*Advisory Information*

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 7:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

Jon M. Lockard, Ph.D.
October 12, 2006

BRENDA BRUMBACK
SUPERVISORY PATENT EXAMINER
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